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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,799	06/20/2001	Ching-Yu Lin	4712-117 US	4493

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EXAMINER
MYERS, CARLA J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/23/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,799	LIN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5 and 13-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5, 13-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. This action is in response to Paper No. 8, filed October 9, 2002. Applicants arguments presented in the response of Paper No. 8 have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

2. Applicant's election with traverse of Claims 1-13, with respect to SEQ ID NO :317, 318, 488 and 490 and HPV 58 probes that hybridize to the region of nucleotides 6608-7016 and HPV 70 probes that hybridize to the region of 6549-6963 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that restriction to 2 oligonucleotide species is improper because it would require 1,444 tests to analyze a patient for risk of papilloma virus if the tests were done using only two oligonucleotides. However, Applicants claims are limited to such tests. If applicant believes that tests can only be performed when all the stated oligonucleotides are used simultaneously, the claims should be amended to read the "detector" contains each and everyone of the stated probes. Since Applicants have chosen to claim a detector that uses only 2 oligonucleotides, Applicant is required to elect 2 oligonucleotides. Applicants stated that a single search is required to evaluate the novelty of the claim. This argument is confusing. Applicants have not clearly pointed out how a search of SEQ ID NO: 1 would lead the examiner to all references teaching SEQ ID NO: 2-646. Clarification is required. If Applicant believes that all of the recited sequences are obvious over one another, such that a reference teaching any papilloma

virus type-specific oligonucleotide would render each of the claimed oligonucleotides obvious, then the record should be clarified to state this opinion.

The requirement is still deemed proper and is therefore made FINAL.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Taiwan on April 5, 2001. It is noted, however, that applicant has not filed a certified copy of the 90110785 application as required by 35 U.S.C. 119(b). Applicants state that a certified translation will be provided upon the allowance of the claims. However, the claims will not be allowed until the certified copy has been received. It is pointed out that the examiner has **not** requested a certified **translation** of the priority document. The requirement is for a certified copy of the priority document which is in fact necessary if Applicants intend to claim priority to this document.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 5, 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Doorn.

Van Doorn et al discloses methods for detecting specific HPV subtypes wherein the methods comprise amplifying nucleic acids contained in a sample with primers specific for HPV;

contacting the amplified nucleic acids with a solid support which has attached thereto probes specific for at least 2 HPV subtypes; and detecting hybridization between said probes and amplified nucleic acids as indicative of the presence of a specific HPV subtype (see, for example, page 4 and Figure 10). In particular, the probes are specific for a single HPV subtype, including HPV 58 and HPV 70 (page 6). The probes are complementary to a region of HPV which includes a portion of the L1 gene that contains a high level of sequence variability, referred to therein as region D (page 7-8). The HPV subtype specific probes are immobilized onto a solid support as parallel lines to allow for the simultaneous detection of multiple HPV subtypes (pages 9 and 16). In reference to claims 2 and 5, Van Doorn teaches that the probe may be immobilized onto a nylon membrane or onto a chip (page 14). The claims are inclusive of oligonucleotides "complementary" to SEQ ID NO: 317, 318, 488 or 490. Because the term "complementary" has not been defined in the specification, this term is considered to be inclusive of oligonucleotides sharing any level of complementarity with the recited sequence. The HPV 58 and HPV 70 probes of Van Doorn share some level of complementarity with SEQ ID NO: 317, 318, 488 and 489 and thereby are considered to be encompassed by the claims. This aspect of the rejection may be overcome by amendment of the claim to recite, for example, "and oligonucleotides fully complementary thereto". With respect to claim 13, the rejection applies to this claim based on the interpretation that the claim includes a method of detection wherein the HPV sequence is any sequence from HPV 58 or HPV 70 since the claim is inclusive of oligonucleotides sharing any

level of sequence identity with the recited sequences. Additionally, Van Doorn teaches labeling the amplified DNA with biotin (see, for example, page 50). Accordingly, Van Doorn teaches a detector comprising a first and second oligonucleotide bound to a carrier wherein the first and second oligonucleotide hybridize with a first and second subtype of HPV and methods for detecting and identifying a first and second subtype of HPV.

RESPONSE TO ARGUMENTS:

In the response of Paper No. 8, Applicants state that Van Doorn does not disclose any of the specific oligonucleotides claimed. However, the claims are not limited to specific oligonucleotides. Rather, the claims are inclusive of oligonucleotides sharing any level of sequence complementarity with the recited sequences of claim 1 and oligonucleotides containing any 15 to 30 nucleotide fragment that shares any level of sequence complementarity with the recited oligonucleotides of claim 13.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorn in view of Southern et al (5,700,637).

Van Doorn et al discloses methods for detecting specific HPV subtypes wherein the methods comprise amplifying nucleic acids contained in a sample with primers specific for HPV; contacting the amplified nucleic acids with a solid support which has attached thereto probes specific for at least 2 HPV subtypes; and detecting hybridization between said probes and amplified nucleic acids as indicative of the presence of a specific HPV subtype (see, for example, page 4 and Figure 10). In particular, the probes are specific for a single HPV subtype, including HPV 58 and HPV 70 (page 6). The probes are complementary to a region of HPV which includes a portion of the L1 gene that contains a high level of sequence variability, referred to therein as region D (page 7-8). The HPV subtype specific probes are immobilized onto a solid support as parallel lines to allow for the simultaneous detection of multiple HPV subtypes (pages 9 and 16). The claims are inclusive of oligonucleotides "complementary" to SEQ ID NO: 317, 318, 488 or 490. Because the term "complementary" has not been defined in the specification,

this term is considered to be inclusive of oligonucleotides sharing any level of complementarity with the recited sequence. The HPV 58 and HPV 70 probes of Van Doorn share some level of complementarity with SEQ ID NO: 317, 318, 488 and 490 and thereby are considered to be encompassed by the claims.

With respect to claim 3, Van Doorn (page 50) teaches immobilizing the probes onto a nitrocellulose or nylon membrane, a microtitre plate, bead or onto a chip, but does not teach immobilizing the probes onto glass.

Southern teaches methods for simultaneously detecting multiple nucleic acids using probes attached to a solid support. Southern teaches that the probes may be attached to any type of solid support, including a glass plate (see, for example, column 1). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Van Doorn so as to have immobilized the probes onto a glass plate rather than a membrane, microtitre plate, bead or chip because this would have provided an equally effective means for immobilizing the probes and for allowing for the simultaneous detection of HPV subtypes.

With respect to claim 18, Van Doorn does not teach labeling the HPV nucleic acids with a fluorescent label. However, Southern teaches labeling probes with fluorescent moieties. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Van Doorn so as to have used a fluorescent label in place of biotin

or digoxigenin in order to have provided an equally effective means for detecting the hybridization complex formed between the HPV nucleic acids and HPV subtype specific probes.

RESPONSE TO ARGUMENTS:

In the response of Paper No. 8, Applicants state that the combined references do not teach or suggest any of the specific oligonucleotides claimed. However, the claims are not limited to specific oligonucleotides. Rather, the claims are inclusive of oligonucleotides sharing any level of sequence complementarity with the recited sequences of claim 1 and oligonucleotides containing any 15 to 30 nucleotide fragment that shares any level of sequence complementarity with the recited oligonucleotides of claim 13.

5. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorn in view of Bauer et al (U.S. Patent No. 5,639,871).

Van Doorn et al discloses methods for detecting specific HPV subtypes wherein the methods comprise amplifying nucleic acids contained in a sample with primers specific for HPV; contacting the amplified nucleic acids with a solid support which has attached thereto probes specific for at least 2 HPV subtypes; and detecting hybridization between said probes and amplified nucleic acids as indicative of the presence of a specific HPV subtype (see, for example, page 4 and Figure 10). In particular, the probes are specific for a single HPV subtype, including HPV 58 and HPV 70 (page 6). The probes are complementary to a region of HPV which includes a portion of the L1 gene that contains a high level of sequence variability, referred to

therein as region D (page 7-8). The HPV subtype specific probes are immobilized onto a solid support as parallel lines to allow for the simultaneous detection of multiple HPV subtypes (pages 9 and 16). The claims are inclusive of oligonucleotides "complementary" to SEQ ID NO: 317, 318, 488 or 490. Because the term "complementary" has not been defined in the specification, this term is considered to be inclusive of oligonucleotides sharing any level of complementarity with the recited sequence. The HPV 58 and HPV 70 probes of Van Doorn share some level of complementarity with SEQ ID NO: 317, 318, 488 and 490 and thereby are considered to be encompassed by the claims.

Van Doorn (page 50) teaches detecting biotin labeled HPV nucleic acids using a streptavidin-alkaline phosphatase reaction system. Van Doorn does not teach detecting biotin labeled HPV nucleic acids using an avidin-alkalinephosphatase reaction system. However, Bauer teaches detecting biotin-labeled HPV nucleic acids using an avidin-alkalinephosphatase detection system. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used avidin-alkalinephosphatase in place of streptavidin-alkalinephosphatase because this would have provided an equally effective means for detecting the hybridization between the HPV nucleic acids and HPV subtype specific probes.

6. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorn in view of Hyldig-Nielsen et al (U.S. Patent No. 5,888,733).

Van Doorn et al discloses methods for detecting specific HPV subtypes wherein the methods comprise amplifying nucleic acids contained in a sample with primers specific for HPV; contacting the amplified nucleic acids with a solid support which has attached thereto probes specific for at least 2 HPV subtypes; and detecting hybridization between said probes and amplified nucleic acids as indicative of the presence of a specific HPV subtype (see, for example, page 4 and Figure 10). In particular, the probes are specific for a single HPV subtype, including HPV 58 and HPV 70 (page 6). The probes are complementary to a region of HPV which includes a portion of the L1 gene that contains a high level of sequence variability, referred to therein as region D (page 7-8). The HPV subtype specific probes are immobilized onto a solid support as parallel lines to allow for the simultaneous detection of multiple HPV subtypes (pages 9 and 16). The claims are inclusive of oligonucleotides "complementary" to SEQ ID NO: 317, 318, 488 or 490. Because the term "complementary" has not been defined in the specification, this term is considered to be inclusive of oligonucleotides sharing any level of complementarity with the recited sequence. The HPV 58 and HPV 70 probes of Van Doorn share some level of complementarity with SEQ ID NO: 317, 318, 488 and 490 and thereby are considered to be encompassed by the claims.

With respect to claims 18 and 19, Van Doorn does not teach labeling the HPV nucleic acids with a fluorescent label and particularly does not teach using a Cyanine 5 label. Hylidig-Nielsen (column 10) teaches methods for labeling nucleic acids and specifically teaches labeling

nucleic acids with the fluorescent label Cyanine 5, as well as labeling nucleic acids with biotin or digoxigenin. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Van Doorn so as to have labeled the HPV nucleic acids with Cyanine-5 because this would have provided an equally effective means for labeling and detecting HPV nucleic acids.

7. Claims 1, 2, 5, 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorn in view of Bauer et al (U.S. Patent No. 5,639,871) and Orth (U.S. Patent No. 5,981,173).

This rejection is based on the interpretation that the claims are inclusive of detectors and methods in which the first oligonucleotide is complementary to SEQ ID NO: 317 or 318 or hybridizes to a region that encompasses or flanks a portion of HPV 58 comprising SEQ ID NO: 317 or 318 and in which the second oligonucleotide is complementary to SEQ ID NO: 488 or 490 or hybridizes to a region that encompasses or flanks a portion of HPV 70 comprising SEQ ID NO: 488 or 490.

Van Doorn et al discloses methods for detecting specific HPV subtypes wherein the methods comprise amplifying nucleic acids contained in a sample with primers specific for HPV; contacting the amplified nucleic acids with a solid support which has attached thereto probes specific for at least 2 HPV subtypes; and detecting hybridization between said probes and amplified nucleic acids as indicative of the presence of a specific HPV subtype (see, for example, page 4 and Figure 10). In particular, the probes are specific for a single HPV subtype, including

HPV 58 and HPV 70 (page 6). The probes are complementary to a region of HPV which includes a portion of the L1 gene that contains a high level of sequence variability, referred to therein as region D (page 7-8). The HPV subtype specific probes are immobilized onto a solid support as parallel lines to allow for the simultaneous detection of multiple HPV subtypes (pages 9 and 16). With respect to claim 4, the claims are inclusive of oligonucleotides "complementary" to SEQ ID NO: 317, 318, 488 or 490. Because the term "complementary" has not been defined in the specification, this term is considered to be inclusive of oligonucleotides sharing any level of complementarity with the recited sequence. Van Doorn does not specifically teach probes comprising SEQ ID NO: 317, 318, 488 or 490 or probes which hybridize to a region comprising or flanking SEQ ID NO: 317, 318, 488 or 490.

Bauer teaches probes specific for HPV 58 wherein the probes consist of the sequence GCACTGAAGTAACTAAGGAAGG and sequences complementary thereto (see SEQ ID NO: 220 of Bauer). The complementary probe of Bauer is complementary to instant SEQ ID NO: 317 and 318 and hybridizes to a region of HPV 58 that encompasses SEQ ID NO: 317 and 318. Furthermore, the probe of Bauer differs from instant SEQ ID NO: 317 in that it is missing 2 5' nucleotides and contains 4 additional 3' nucleotides. The probe of Bauer also differs from instant SEQ ID NO: 318 in that contains 1 additional 5' nucleotide and 1 additional 3' nucleotide. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the probes of Bauer so as to have added or deleted nucleotides from

the 5' or 3' terminus and to have thereby generated additional probes for specifically detecting HPV 58, including probes consisting of instant SEQ ID NO: 317 and 318. It would have been well within the skill of the art at the time the invention was made to have modified the probes of Bauer in such a manner since the sequences for HPV 58 and related HPV subtypes were well known in the art and because Bauer provides extensive guidance for modifying probes and for selecting additional probes specific for HPV 58.

Furthermore, with respect to HPV 70 probes, Orth teaches the complete sequence of the HPV 70 genome, including L1 sequences comprising instant SEQ ID NO: 488 and 490 (see SEQ ID NO: 11 of Orth). In addition, Van Doorn and Bauer each teach generating HPV subtype specific probes by comparing the L1 region of HPV subtypes and identifying those sequences within that are unique to a particular HPV subtype. The prior art also teaches the complete sequence of L1 for HPV subtypes. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have generated HVP 70 specific probes complementary to the L1 region in order to have to provided additional probes that specifically detect HPV. Again, it is noted that this aspect of the rejection as it pertains to HPV70 probes is applied to the claims to the extent that they are not limited to oligonucleotides of a specific sequence, but rather include probes which share some level of sequence complementarity with SEQ ID NO: 488 or 490 and include probes which hybridize to regions of HPV 70 comprising or flanking the sequences of SEQ ID NO: 488 or 490.

With respect to newly added claim 17, Van Doorn (page 50) teaches detecting biotin labeled HPV nucleic acids using a streptavidin-alkalinephosphatase reaction system. Van Doorn does not teach detecting biotin labeled HPV nucleic acids using an avidin-alkalinephosphatase reaction system. However, Bauer teaches detecting biotin-labeled HPV nucleic acids using an avidin-alkalinephosphatase detection system. Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used avidin-alkalinephosphatase in place of streptavidin-alkalinephosphatase because this would have provided an equally effective means for detecting the hybridization between the HPV nucleic acids and HPV subtype specific probes.

RESPONSE TO ARGUMENTS:

In the response of Paper No. 8, Applicants state that the combined references do not teach or suggest any of the specific oligonucleotides claimed. However, the claims are not limited to specific oligonucleotides. Rather, the claims are inclusive of oligonucleotides sharing any level of sequence complementarity with the recited sequences of claim 1 and oligonucleotides containing any 15 to 30 nucleotide fragment that shares any level of sequence complementarity with the recited oligonucleotides of claim 13. Additionally, Applicants arguments do not address why the cited references do not render the claimed oligonucleotides obvious. The cited prior art teaches oligonucleotides that differ from the claimed oligonucleotides only in that they contain additional 3' or 5' nucleotides. In particular, the probe of Bauer differs from instant SEQ ID NO:

317 in that it is missing two 5' nucleotides and contains four additional 3' nucleotides. The probe of Bauer also differs from instant SEQ ID NO: 318 in that contains one additional 5' nucleotide and one additional 3' nucleotide. The oligonucleotides of Bauer have the same functional activity as the claimed oligonucleotides, that is they are specific for HPV 58 and HPV 70 and they hybridize to the same regions of HPV 58 and 70 as the claimed oligonucleotides.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANTS AMENDMENTS TO THE CLAIMS AND SPECIFICATION:

9. Claims 3 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorn in view of Bauer and Orth and further in view of Southern et al (5,700,637).

The teachings of Van Doorn, Bauer and Orth are presented in paragraph 8 above.

With respect to claim 3, Van Doorn (page 50) teaches immobilizing the probes onto a nitrocellulose or nylon membrane, a microtitre plate, bead or onto a chip, but does not teach immobilizing the probes onto glass.

Southern teaches methods for simultaneously detecting multiple nucleic acids using probes attached to a solid support. Southern teaches that the probes may be attached to any type of solid support, including a glass plate (see, for example, column 1). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Van Doorn so as to have immobilized the probes onto a glass plate rather than a membrane, microtitre plate, bead or chip because this would have provided an equally effective

means for immobilizing the probes and for allowing for the simultaneous detection of HPV subtypes.

With respect to claim 18, Van Doorn does not teach labeling the HPV nucleic acids with a fluorescent label. However, Southern teaches labeling probes with fluorescent moieties. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Van Doorn so as to have used a fluorescent label in place of biotin or digoxigenin in order to have provided an equally effective means for detecting the hybridization complex formed between the HPV nucleic acids and HPV subtype specific probes.

RESPONSE TO ARGUMENTS:

In the response of Paper No. 8, Applicants state that the combined references do not teach or suggest any of the specific oligonucleotides claimed. However, the claims are not limited to specific oligonucleotides. Rather, the claims are inclusive of oligonucleotides sharing any level of sequence complementarity with the recited sequences of claim 1 and oligonucleotides containing any 15 to 30 nucleotide fragment that shares any level of sequence complementarity with the recited oligonucleotides of claim 13.

10. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Doorn in view of Bauer and Orth and further in view of Hyldig-Nielsen et al (U.S. Patent No. 5,888,733).

The teachings of Van Doorn, Bauer and Orth are presented in paragraph 8 above. The combined references do not teach labeling the HPV nucleic acids with a fluorescent label and particularly does not teach using a Cyanine 5 label. Hylidig-Nielsen (column 10) teaches methods for labeling nucleic acids and specifically teaches labeling nucleic acids with the fluorescent label Cyanine 5, as well as labeling nucleic acids with biotin or digoxigenin. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have further modified the method of Van Doorn so as to have labeled the HPV nucleic acids with Cyanine-5 because this would have provided an equally effective means for labeling and detecting HPV nucleic acids.

11. The amendment filed October 9, 2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The specification has been amended to add new sequences consisting of SEQ ID NO: 651-688. The specification as originally filed does not provide support for these sequences. Applicants response filed October 9, 2002 indicates that the added sequences correspond to NCBI Accession Numbers. However, the sequences in the NCBI database are continuously modified and updated. Applicants have not provided any declaratory evidence to show that the newly added sequences are identical to the sequences that were present in the NCBI database as of the filing date of the present application.

Applicant is required to cancel the new matter in the reply to this Office Action.

12. Claims 13-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the sequences of SEQ ID NO: 651-566 recited in claims 13-19. The specification as originally filed disclosed 650 sequences. The newly added sequences are not supported in the original disclosure. As stated above, the response filed October 9, 2002 does not provide declaratory evidence showing that the newly added sequences are identical to the sequences that were present in the NCBI database as of the filing date of the present application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

CARLA J. MYERS
PRIMARY EXAMINER

December 16, 2002